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ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,469	TACHIBANA, HIROFUMI	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,12,13,16,17 and 33-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 12-13, 16-17, 33-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant cancels claims 2, 14-15, 31-32 and adds new claims 35-38.

Accordingly, claims 1, 12-13, 16-17, 33-38 are examined in the instant application.

Withdrawn Rejection

The following rejections have been withdrawn: 112, second paragraph, in view of the amendment.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 12-13, 16-17 and 33-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, for reasons already of record in paper of 07/23/08.

The response asserts as follows:

As Hou et al., 2004 points out, the anticancer effect of catechins including EGCG have previously been tested with concentrations that are significantly higher than physiological concentrations. In contrast, the concentrations of EGCG used in the development of the anti-cancer assays of the present invention were much lower physiological concentrations (0.1 mM and 1 raM). Employing these concentrations, the inventor identified the 67 kDa laminin receptor

as a molecule which is essential for EGCG to exhibit an effect on or inhibit cancer cell proliferation.

Based on this finding, it has already been proven by in vivo testing that the anti-cancer effect of EGCG can be shown against cancer cells expressing the 67 kDa laminin receptor. (See attached publication to Umeda et al., Journal of Biological Chemistry, 2008, 283: 3050-3058). Considering this finding, the in vitro effect can be extrapolated to the in vivo effect in this case. That is, one skilled in the art can expect, based on positive in vitro screening results obtained with a compound using the 67 kDa laminin receptor according to the practice of the present invention, that the compound will display anti-cancer effects in vivo.

Further, the invention are not directed to methods of cancer therapy. Rather, they are directed to methods of screening compounds that may have a cell growth-inhibiting effect or a cancer cell metastasis activity-inhibiting effect.

The submission of Umeda et al is acknowledged.

The response has been considered but is not found to be persuasive for the following reasons:

Although the specification is enabled for a method for screening a catechin or antibody that has in vivo cell inhibiting effect on melanoma, or in vitro cell inhibiting effect on lung cancer cells in culture, wherein said catechin or antibody displaces the binding of epigallocatechin gallate to the full length 67 kDa laminin receptor expressed on the cell surface of melanoma or lung cancer cells, wherein the antibody displaces the binding of laminin to the 67kDa laminin receptor, the specification is not enabled for screening a catechin or antibody that has in vivo or in vitro cell inhibiting effect on any cancer cells, wherein said catechin or antibody

merely binds to the 67 kDa laminin receptor, or merely bind to the same site as that of any compound that has a galloyl group, or the same site as that epigallocatechin gallate, and wherein said receptor does not have to be expressed on the cancer cell surface, and could be in a solution, comprising a purified protein, a soluble protein, a purified protein bound to a carrier, or to another protein, or a partial peptide of 37 kDa.

One cannot extrapolate from a single disclosure of **in vivo killing** of melanoma cells, taught by Umeda, and in vitro killing of a lung cancer cell line, as disclosed in the specification, by epigallocatechin gallate to in vivo killing of **any other cancers** by said compound, or metastatic cancer cells, because different cancers have different etiology and properties and do not predictably response the same way to the same drug, and because results of an in vitro assay cannot predictably be the same as those in vivo, in view of the teaching of Zips et al, Lee et al, Kirkin et al, Kimmel et al, and Dermer, all of record. Further, cell growth inhibiting effect encompasses inhibiting growth of any cells, including healthy, **non-cancerous** cells. One cannot predict that growth of any cells, including non-cancerous cells would be inhibited by the compounds screened by the claimed method, because one cannot predict that any cells, including non-cancerous cells, overexpress the laminin receptor. As taught by Umeda et al, 2008, submitted in the response, the 67 kDa laminin receptor is overexpressed in various cancer cells (p. 3050, second column, second paragraph).

Further, one cannot predict that a catechin or an antibody that **merely binds** to the 67 kDa laminin receptor, as claimed in claims 1, 35-38, would have the property of epigallocatechin gallate (EGCG), activate a signal pathway specific for EGCG, and kill melanoma or lung cancer cells, because binding perse to the receptor, for example, by the ligand laminin does not activate

said pathway. As taught by Umeda, 2008, submitted in the response, epigallocatechin-3- gallate (EGCG) kills melanoma cells via a specific signaling pathway through activation of the 67 kDa laminin receptor (abstract). Said signaling pathway, via eEF1A activation, dephosphorylation of myosin phosphatase targeting subunit 1, and activation of myosin phosphatase, is perculiar to EGCG, because binding of the ligand laminin to said receptor does not activate said particular signaling pathway (abstract, p.3057, first column, second paragraph).

Similarly, one cannot predict that an antibody that merely binds to the 67kDa laminin receptor at any position of the receptor would have the property of the antibody taught by Narumi et al, of record, and displaces the laminin ligand, because one cannot predict that the screened antibody would have the same epitope as that of the antibody taught by Narumi et al. Different from EGCG, the antibody taught by Namura et al, of record, prevents attachment and migration of lung cancer cells to laminin-coated surfaces, and metastasis by lung cancer cells in vivo, by displacing the binding of the ligand laminin to the receptor (abstract, p.428).

In addition, one cannot predict that **any compounds having a galloyl group** could be used as a control, and has cell growth inhibiting activity or cancer cell metastasis inhibiting effect, as claimed in claims 12-13, 16-17, 33-34. The response, however, does not address this issue. One cannot predict that said compound would have the same property as epigallocatechin gallate, in view that: 1) one cannot predict whether the galloyl moiety per se is responsible for the cell killing property of epigallocatechin gallate, such as capable of displacing the binding of epigallocatechin gallate to the 67 kDa laminin receptor, or whether the galloyl moiety only contributes the configuration of EGCG, necessary for fitting into the receptor, and 2) the site or domain of epigallocatechin gallate that is responsible for its binding to the 67 kDa laminin

receptor and inducing eEF1A activation, dephosphorylation of myosin phosphatase targeting subunit 1, and activation of myosin phosphatase is not disclosed in the specification.

Similarly, one cannot predict that other than EGCG, EGCG"3Me, and ECG, there exists a compound that has as part of its structure, the moiety galloyl, has a configuration that would be recognized by the laminin receptor and fit into the receptor structure to activate the receptor. It is noted that a ligand, whether it is an agonist or antagonist, has to have a certain binding stability, and has to have molecular configuration specificity, for example, a certain configuration for perfect fit into the receptor, like lock and key. In addition, not any catechins bind to and inhibit the laminin receptor, as shown by, for example, the catechins epigallocatechin (EGC) and epicatechin (EC), as disclosed in the specification (p.43).

In addition, one cannot predict that a compound that **merely binds to the site of the binding** of epigallocatechin gallate (EGCG), as claimed in claim 34, would have the property of EGCG, because one cannot predict whether said compound has sufficient affinity to the 67 kDa laminin receptor to be stable, and/or the configuration necessary to fit into the receptor, and activate the receptor.

Moreover, the 67 kDa laminin receptor **expressed from a vector**, as claimed in claim 1, or without being specified to be tested on cancer cell surface, as claimed in claims 12-13, 16-17, 33-38, encompasses a 67 kDa laminin receptor **in a solution** and not necessarily on cancer cell surface. One cannot predict that said receptor used in the claimed method would have a configuration necessary for testing its function, or its binding to the catechin and the displacement of EGCG by said catechin, in view that the 67kDa laminin receptor seems to need the cell membrane environment for its structure and function. The instant specification discloses

that 67 kDa laminin receptor (hereinafter it may be referred to as "67LR") is a protein of 67 kDa, which is derived from a 37 kDa precursor protein translated from mRNA that codes for 295 amino acids, through intracellular acylation polymerization of the precursor protein by a fatty acid for homo-dimerization or hetero-dimerization thereof; and only when it moves onto the surface of a cell membrane together with integlins, it functions as a laminin receptor (Biochemistry, 1995, 34: 11276-11287, T. H. Landowski et al.; J. Cell. Biochem., 1998, 69: 244-251, S. Buto et al.) (p.1). Further, one cannot predict that the claimed 67 kDa laminin receptor in a form of a **soluble protein, a protein bound to a carrier or cell surface, a protein fused with another protein, or its precursor, a partial peptide of 37 kDa** (the instant specification, p.1), as claimed in claim 35, would be suitable for the claimed method for screening **catechin**, and would have the size and configuration necessary for its activity, such as inducing eEF1A activation, dephosphorylation of myosin phosphatase targeting subunit 1, and activation of myosin phosphatase, in view of the above teaching, which indicates that a full length homo- or hetero-dimerized 67 kDa laminin receptor, situated on a surface of a cancer cell membrane environment is required for its structure and function. Moreover, the ability of the tested soluble receptor, or partial peptide of 37 kDa to bind to laminin is not sufficient to confer the cancer cell killing effect by a catechin, in view of the above teaching of Umeda et al, supra, that binding of the ligand laminin to the 67 kDa receptor does not activate the particular signaling pathway necessary for the catechin EGCG to kill cancer cells . In addition, it is not clear what is the partial peptide of 37 kDa, as claimed in claim 35, which is not necessarily a fragment of the 67 kDa laminin receptor.

Moreover, the antibody as claimed in claims 37-38 cannot be a compound in claim 12, which has a galloyl group, because there is no evidence that a natural antibody has a galloyl group. Further, the specification does not teach such antibody for use as a control in the claimed method, nor how to make such antibody, such that it has the property of EGCG.

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the claimed invention, there would be an undue quantity of experimentation required for one of skill in the art to practice the claimed invention, that is commensurate in scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 remains rejected under 35 U.S.C. 102(b) as being anticipated by Narumi et al, 1999, Jpn J Cancer Res, 90: 425-431, IDS of 04/26/07, for reasons already of record in paper of 07/23/08.

The response asserts as follows:

Claim 1 has been amended to recite that the 67 kDa laminin receptor is expressed from a gene expression vector.

Narumi teaches exposing cells from the human sarcoma cell line H1080 to an antibody against a 37kDa partial peptide fusion protein. 67kDa LR from these cells is not expressed from a gene expression vector. Therefore, Narumi does not anticipate the claimed subject matter.

The response has been considered but is not found to be persuasive for the following reasons: The 67 kDa laminin receptor expressed from a gene expression vector, as claimed in claim 1, is interpreted as product by process, and thus is the same as the product.

Because the method of the prior art comprises the same method steps as claimed in the instant invention using the same composition, the claimed method is anticipated because the method will inherently lead to the claimed effects. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

New Rejection Due to the Amendment

Claim Rejections - 35 USC § 112 First Paragraph, New Matter

Claims 37-38 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention.

The limitation of an antibody compound having a galloyl group as claimed in claims 37-38 has no clear support in the specification and the claims as originally filed. A review of the specification discloses support for a monoclonal antibody to the 67 kDa laminin receptor, that interferes with the binding of a compound having a galloyl group (p.26, second paragraph).

There is nothing in the specification to suggest or disclose an antibody that has galloyl group. In the instant application, the original disclosure of a compound having a galloyl group does not support a later filed claim to a species antibody having the galloyl group.

The original disclosure of a large genus did not support a later filed claim to a previously unnamed single species. In re Ruschig, 371 F.2d 990, 154 USPQ 118 (CCPA 1967). See also Purdue Pharma L.P. v. Faudling Inc., 230 F.3d 1320, 1326, 56 USPQ2d 1481, 1486 (Fed. Cir. 2000).

The subject matter claimed in claims 37-38 broadens the scope of the invention as originally disclosed in the specification.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 12-13, 16-17, 33-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 12-13, 16-17, 33-38 are indefinite for the use of the relative term "may" in claims 1, 12-13, 35-36, which does not set the metes and bounds of the claimed invention.

Claim Rejections - 35 USC § 102

Claim 35 is rejected under 35 U.S.C. 102(b) as being anticipated by Narumi et al, 1999, Jpn J Cancer Res, 90: 425-431, IDS of 04/26/07, as evidenced by the instant specification, p.1.

Claim 35. (New) A method of screening a catechin or antibody that may have a cell growth-inhibiting effect or a cancer cell metastasis activity-inhibiting effect, which comprises the steps of

qualitatively or quantitatively determining the degree of binding of the catechin or antibody to a 67 kDa laminin receptor, and, when the catechin or antibody binds to the 67 kDa laminin receptor, then

judging that the catechin or antibody may have a cell growth-inhibiting effect or a cancer cell metastasis activity-inhibiting effect,

wherein the 67 kDa laminin receptor is in a form selected from the group consisting of a purified protein, a soluble protein, a protein bound to a carrier or cell surface, a protein fused with another protein, and a partial peptide of 37 kDa that has the ability to bind to laminin.

Narumi et al teach testing of an antibody for its binding to the 67 kDa laminin receptor, and its effect on metastasis of human lung fibrosarcoma cells (abstract, p.425, second column, p.426, second column, p427, first column, paragraph before the results). Namuri et al also teach that the antibody is generated from the 37 kDa precursor protein (p.425).

Although Narumi et al do not teach that the 67 kDa laminin receptor is bound to a cell surface, it is the inherent property of the 67 kDa receptor to be expressed on the cell surface, as disclosed in the instant specification. The instant specification discloses that the 67 kDa laminin receptor (hereinafter it may be referred to as "67LR") is a protein of 67 kDa, which is derived from a 37 kDa precursor protein translated from mRNA that codes for 295 amino acids, through intracellular acylation polymerization of the precursor protein by a fatty acid for homo-dimerization or hetero-dimerization thereof; and only when it moves onto the surface of a cell membrane together with integlins, it functions as a laminin receptor (Biochemistry, 1995, 34: 11276-11287, T. H. Landowski et al.; J. Cell. Biochem., 1998, 69: 244-251, S. Buto et al.) (the instant specification, p.1).

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
December 17, 2008

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643